PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No.	International Filing Date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/AU2003/001118	29 August 2003	30 August 2002

International Patent Classification (IPC) or national classification and IPC

Int. Cl.[7] C07H 21/04, C12Q 1/68, C12M 1/34, B82B 1/00, B82B 3/00

Applicant

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 7 sheet(s).

3. This report contains indications relating to the following items:

   I [X] Basis of the report

   II [ ] Priority

   III [ ] Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

   IV [ ] Lack of unity of invention

   V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI [X] Certain documents cited

   VII [ ] Certain defects in the international application

   VIII [ ] Certain observations on the international application

Date of submission of the demand	Date of completion of the report
23 March 2004	8 December 2004
Name and mailing address of the IPEA/AU	Authorized Officer
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/001118

Basis of the report

With regard to the elements of the international application:*

☐ the international application as originally filed.

☒ the description, pages **1-2, 6-104, 117** as originally filed,
pages , filed with the demand,
pages **3-5, 5a** received on **30 November 2004** with the letter of **30 November 2004**

☒ the claims, pages **108-116** as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages **105-107,** received on **30 November 2004** with the letter of **30 November 2004**

☒ the drawings, pages **1/27-27/27** as originally filed,
pages , filed with the demand,
pages , received on with the letter of

☐ the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages

☐ the claims, Nos.

☐ the drawings, sheets/fig.

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-8, 10-52	YES
	Claims	9	NO
Inventive step (IS)	Claims		YES
	Claims	1-52	NO
Industrial applicability (IA)	Claims	1-52	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1 Chen R J et al, J. Am. Chem. Soc. 2001, 123, pp 3838-3839

D2 Tsang S C et al, Angew. Chem. Int. Ed. Engl. 1997, 36 No 20, pp2198-2200

D3 WO 1997032571

D4 WO 2002095099

D5 US 2002/0172963

D6 US 6555362

D7 Williams K A et al, Nature 2002 vol 420 page 761.

D8 Service R F, Science 2002 vol 298 pp 2322-2323

D9 Hazani M et al, Nano Letters 2003 vol 3 no 2 pp 153-155

D10 Baker S E et al, Nano Letters 2002 vol 2 no 12 pp 1413-1417

D11 Stevens J L et al, Nano Letters 2003 vol 3 no 3 pp 331-336

D12 Cai H etal, Anal Bioanal Chem 2003 vol 375 pp 287-293

D13 Williams K A et al, AIP Conference Proceedings (2002) 633 (Structural and Electronic Properties of Molecular Nanostructures), pp 444-448

D4-D13 are published prior to the international filing date but later than the priority date claimed and are therefore not relevant in the consideration of novelty or inventive step. These documents may become relevant if the priority date claimed by the instant application is found to be invalid.

D1 discloses a bifunctional molecule physically adsorbed onto the surface of single-walled carbon nanotubes (SWNTs) and then linked to a protein. DNA molecules adsorbed on MWNTs via non-specific interactions were also disclosed. Given the state of the art, no inventive step can be acknowledged by attaching a different biomolecule, ie, DNA, to the carbon nanotube using its known properties. Therefore, claims 1-52 are not inventive.

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
WO 2002095099	28 November 2002	29 March 2002	29 March 2001
US 2002/0172963	21 November 2002	9 January 2002	10 January 2001
US 6555362	29 April 2003	10 October 2001	30 May 2001

WO 2002095099 discloses that non-covalently bonded molecules are configured and arranged for bonding to, for example, DNA and proteins, on SWNTs and a plurality of SWNTs are provided for the functionalisation, see page 3 lines 9-16, page 5 line 9 to page 6 line 5, page 7 lines 3-20, claim 13 and figure 1.

US 2002/0172963 discloses an array of carbon nanotubes to which biological molecules including DNA and RNA are attached.

US 655362 discloses an apparatus for determining gene sequences based on the detection of attractive force associated with specific complementary hydrogen bonding between each type of nucleotide base with a probe consisting of carbon nanotubes bound with nucleotides.

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

Supplemental Box
To be used when the space in any of the preceding boxes is not sufficient)

Continuation of **Box V**

D2 discloses the immobilisation of DNA oligomers on carbon nanotubes by adsorption. It also discloses anchoring DNA onto a solid surface so that it functions as a chemical recognition agent for complementary DNA. Given the state of the art, no inventive step can be acknowledged in attaching nucleic acid to a nanotube. Claims 1-52 are therefore not inventive.

D3 discloses methods for introducing functional groups to the surface of functionalized nanotubes and to nanotubes linked to one another. It also discloses attachment of proteins to the nanotubes, see, for example, Example 21. Other moieties that can be attached to the nanotubes are peptide, enzyme, antibody, oligonucleotide, nucleotide and antigen Claim 9, which is directed to a plurality of linked nanotubes, is not novel in light of the disclosure. The disclosure also renders claims 1-52 not inventive.

Claims 1-52 are considered to have industrial applicability.

nanotubes either side-to-side or end-to-end.

SUMMARY OF THE INVENTION

The inventors have now developed a process capable of linking nanotubes. Importantly, the inventors have developed a process, which allows linkage of nanotubes either side-to-side or end-to-end, thereby dramatically increasing their usefulness. The inventors have also developed a process of physically modifying the walls of nanotubes, while preserving the sp^2 structure of the nanotubes and thus their electronic characteristics. The inventors have also developed a method for locating nanotubes to specific targets. The inventors have also developed techniques which allow DNA patterning on nanotubes as well as the creation of multiple layers of nanoparticles on the surface of nanotubes.

In its broadest aspect, the invention provides a method of chemically attaching nucleic acid molecules to one or more nanotubes. The invention also provides a method of physically attaching nucleic acid molecules to one or more nanotubes. The invention also provides a method of linking these nanotubes. Further, the invention provides a process whereby nanotubes may be directed to specific locations.

Accordingly, in a first aspect, the present invention provides a nanotube with one or more nucleic acid molecule(s) attached thereto.

In a second aspect, the invention provides a method of chemically modifying a nanotube comprising either:

(i) a) chemically attaching at least one linker attached to one or more nucleic acid molecules to an optionally functionalised nanotube, wherein said linker consists wholly or partly of a functional group with the proviso that when the nanotube is functionalised with CO_2H, then the linker is not a primary aliphatic alkyl amine; and

b) synthesising at least two nucleic acid molecules, by sequential addition of nucleotides *in situ*, starting from said one or more nucleic acid molecules; or

(ii) a) chemically attaching at least one linker attached to one or more nucleic acid molecule to an optionally functionalised nanotube, wherein said linker consists wholly or partly of a functional group; and

b) synthesising at least two nucleic acid molecules, by sequential addition of nucleotides *in situ*, starting from said one or more nucleic acid molecules; or

(iii) a) chemically attaching at least one linker to an optionally functionalised nanotube, wherein said linker consists wholly or partly of a functional group; and

b) attaching one or more nucleic acid molecules to said optionally functionalised nanotube via said functional group on said linker; or

(iv) (a) chemically attaching at least one linker to an optionally functionalised nanotube, wherein said linker consists wholly or partly of a functional group; and.

b) synthesising one or more nucleic acid molecules, by sequential addition of nucleotides *in situ*, starting from said functional group on said linker.

In a third aspect, the invention provides a method of chemically modifying a nanotube comprising either:

(i) a) photochemically attaching at least one linker attached to one or more nucleic acid molecules to an optionally functionalised nanotube, wherein said linker consists wholly or partly of a functional group; and

b) synthesising at least two nucleic acid molecules by sequential addition of nucleotides *in situ*, starting from said one or more nucleic acid molecules; or

(ii) a) photochemically attaching at least one linker to an optionally functionalised nanotube, wherein the linker consists wholly or partly of a functional group; and

b) attaching one or more nucleic acid molecules to said optionally functionalised nanotube via said functional group on said linker; or

(iii) a) photochemically attaching at least one linker to an optionally functionalised nanotube, wherein the linker consists wholly or partly of a functional group; and

b) synthesising one or more nucleic acid molecules, by sequential addition of nucleotides *in situ*, starting from said functional group on said linker.

In a fourth aspect, the invention provides a method of physically modifying a nanotube comprising either:

(i) a) physically adsorbing at least one anchor attached to one or more nucleic acid molecules to the surface of an optionally functionalised nanotube, wherein said anchor consists wholly or partly of a functional group;

b) synthesising at least two nucleic acid molecules by sequential addition of nucleotides *in situ*, starting from said functional group on said anchor; or

(ii) a) physically adsorbing at least one anchor to the surface of an optionally functionalised nanotube, wherein said anchor consists wholly or partly of a functional group; and

b) chemically attaching one or more nucleic acid molecules to said functional group on said anchor adsorbed on the optionally functionalised nanotube; or

(iii)a) physically adsorbing at least one anchor attached to one or more nucleic acid molecules to the surface of an optionally functionalised nanotube, wherein said anchor consists wholly or partly of a functional group;

b) synthesising one or more nucleic acid molecules, by sequential addition of nucleotides *in situ*, starting from said functional group on said anchor.

In a fifth aspect, the invention provides a plurality of linked nanotubes.

In a sixth aspect, the present invention provides a method of linking nanotubes comprising the steps of:

a) attaching a first nucleic acid molecule of a first base sequence to a first optionally functionalised nanotube; and

b) hybridizing the first nucleic acid molecule with

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A nanotube with one or more nucleic acid molecule(s) attached thereto.

2. A method of chemically modifying a nanotube comprising either:

(i) a) chemically attaching at least one linker attached to one or more nucleic acid molecules to an optionally functionalised nanotube, wherein said linker consists wholly or partly of a functional group with the proviso that when the nanotube is functionalised with CO_2H, then the linker is not a primary aliphatic alkyl amine; and

b) synthesising at least two nucleic acid molecules, by sequential addition of nucleotides *in situ*, starting from said one or more nucleic acid molecules; or

(ii) a) chemically attaching at least one linker attached to one or more nucleic acid molecule to an optionally functionalised nanotube, wherein said linker consists wholly or partly of a functional group; and

b) synthesising at least two nucleic acid molecules, by sequential addition of nucleotides *in situ*, starting from said one or more nucleic acid molecules; or

(iii)a) chemically attaching at least one linker to an optionally functionalised nanotube, wherein said linker consists wholly or partly of a functional group; and

b) attaching one or more nucleic acid molecules to said optionally functionalised nanotube via said functional group on said linker; or

(iv) a) chemically attaching at least one linker to an optionally functionalised nanotube, wherein said linker consists wholly or partly of a functional group; and

b) synthesising one or more nucleic acid molecules, by sequential addition of nucleotides *in situ*, starting from said functional group on said linker.

3. A method of chemically modifying a nanotube comprising either:

(i) a) photochemically attaching at least one linker attached to one or more nucleic acid molecules to an optionally functionalised nanotube, wherein said linker consists wholly or partly of a functional group; and

(b) synthesising at least two nucleic acid molecules by sequential addition of nucleotides *in situ*, starting from said one or more nucleic acid molecules; or

(ii) a) photochemically attaching at least one linker to an optionally functionalised nanotube, wherein the linker consists wholly or partly of a functional group; and

b) attaching one or more nucleic acid molecules to said optionally functionalised nanotube via said functional group on said linker; or

(iii)a) photochemically attaching at least one linker to an optionally functionalised nanotube, wherein the linker consists wholly or partly of a functional group; and

b) synthesising one or more nucleic acid molecules, by sequential addition of nucleotides *in situ*, starting from said functional group on said linker.

4. A method of physically modifying a nanptube comprising either:

(i) (a) physically adsorbing at least one anchor attached to one or more nucleic acid molecules to the surface of an optionally functionalised nanotube, wherein said anchor consists wholly or partly of a functional group;

b) synthesising at least two nucleic acid molecules by sequential addition of nucleotides *in situ*, starting from said functional group on said anchor; or

(ii) a) physically adsorbing at least one anchor to the surface of an optionally functionalised nanotube, wherein said anchor consists wholly or partly of a

functional group; and

b) chemically attaching one or more nucleic acid molecules to said functional group on said anchor adsorbed on the optionally functionalised nanotube; or

(iii)a) physically adsorbing at least one anchor attached to one or more nucleic acid molecules to the surface of an optionally functionalised nanotube, wherein said anchor consists wholly or partly of a functional group;

b) synthesising one or more nucleic acid molecules, by sequential addition of nucleotides *in situ*, starting from said functional group on said anchor.

5. A method of linking nanotubes comprising the steps of:

a) attaching a first nucleic acid molecule of a first base sequence to a first optionally functionalised nanotube; and

b) hybridising the first nucleic acid molecule with a second nucleic acid molecule of a second base sequence attached on a second optionally functionalised nanotube, wherein the base sequence of the second nucleic acid molecule is substantially complementary to the base sequence of the first nucleic acid molecule.

6. A method of linking nanotubes comprising the steps of:

a) attaching a first nucleic acid molecule of a first base sequence to optionally functionalised nanotubes; and

b) hybridising the first nucleic acid molecule with a second nucleic acid molecule which comprises a base sequence substantially complementary to the first base sequence and further comprises a second or a third base sequence which is/are not complementary to the first base sequence, but is/are complementary to each